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EXAMINER	
WESSENDORF, TERESA D	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/668,778	BALINT ET AL.	
	Examiner	Art Unit	
	TERESA WESSENDORF	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *66 and 71-79* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *66, 71-79* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 64, 66 and 68-79 are pending.

Claims 1-63, 65 and 67 are cancelled.

Claims 64 and 68-70 are withdrawn from further consideration as being drawn to non-elected species.

Claims 66 and 71-79 are under examination.

Priority

Applicants' claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicants have not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 and/or 119(e) as follows:

This application is a CON of 09/526,106 03/15/2000 ('106), which claims benefit of 60/175,968 filed 01/13/2000 ('968) and claims benefit of 60/135,926 filed on 05/25/1999 ('926) and claims benefit of 60/124,339 filed on 03/15/1999 ('339). However, one or more of the applications stated above fail to provide adequate support under 35 U.S.C. § 112, first paragraph for the claimed invention as follows:

> (A) For ***claims 78, 66, 71-7 and 79***, none of the applications provide support for the current genus of fragment complementation systems wherein "fused through a C-terminal residue to a first flexible polypeptide linker and a first interactor domain; and [wherein] said second oligopeptide sequence comprising… a second interactor domain, a second flexible polypeptide linker fused through an N-

terminal residue to a C-terminal fragment of the TEM-1-β-1actamase protein, not less than 25 amino acids in length; (e.g., see New Matter Rejection below).

(B) For **claims 72-77**, the **'339** application fails to provide support for peptides segments that "enhance" functional reconstitution including HSE, EKR, QGN, DGR, GRR, and GNS.

(C) ***For claims 72-77***, the ***'926*** application fails to provide support for peptides segments that "enhance" functional reconstitution including HSE, EKR, QGN, DGR, GRR, and GNS.

If applicant believes this assessment is in error, applicant must disclose where in the specification support for these limitations can be found. See MPEP § 714.02. Therefore the filing date of the instant application is deemed to be its actual filing date, **September 22, 2003**.

Applicant states that this application is a continuation or divisional application of the prior-filed application (see above). A continuation or divisional application cannot include new matter. Applicant is required to change the relationship (continuation or divisional application) to continuation-in-part because this application contains the following matter not disclosed in the prior-filed application: See New Matter rejection below.

Response to Arguments

Applicants state that claim 78 clarifies that the TEM-1- β-1actamase fragment complementation system comprises a first oligopeptide corresponding to an N-terminal fragment of TEM-1-β- 1actamase, and a second oligopeptide corresponding to a C- terminal fragment of TEM-1-β-1actamase, wherein the N-terminal fragment has a C-terminus and the C-terminal

fragment has an N-terminus located within the solvent exposed loop between Thr 195 and Ala 202 of a TEM-1-β-1actamase protein. Support for new claim 78 can be found in the instant application (U.S. Pat. App. No. 10/668,778) and the priority document U.S. Pat. App. No. 09/526,106 filed March 15, 2000, of which the instant application is a continuation. For example, page 11, lines 5-10 of the '106 application (and the instant application as filed state that:

> The combined lengths of the N-terminal fragment and the C-terminal fragment may be discontinuous with residues around the break-point deleted, contiguous, or overlapping with residues around the break-point repeated, thereby comprising from 90% to 100% of the total length of the parent protein. Break-point termini are herein defined as the C-terminus of the N-terminal fragment and the N-terminus of the C- terminal fragment. Emphasis added.

Support for a solvent exposed loop between amino acid residues Thr 195 and Ala 202, can be found in the priority documents as indicated in the prior responses. For example, at page 16, lines 10-13, of the '106 priority document and the instant application as filed states that:

> An exposed loop was identified by this method between two α-helixes of E.coli TEM-I-beta lactamase (approximately Thr195 to Ala 202, between helixes 7 and 8) within which the chain could be broken to produce fragments ....

In reply, the above-quoted sections of the specification regarding claims in newly added claim 78 and the "solvent" exposed loop do not provide for the instant claimed fragment.

New claim 78 does not recite a breakpoint or a discontinuous residue around said breakpoint. Rather, N and C terminal components each with a flexible linker and a first and second reactor domain, interacting respectively.

The above-cited page 16 does not recite a "solvent". The specification recites only identification of an exposed loop. Accordingly the '106 does not provide support for the new amended claim 78.

Applicants argue, with regards to paragraphs B and C above, that Applicants have indicated in the response filed on October 29, 2007, where claims 72-77 are supported by U.S. Provisional App. No: 60/175,968 ('968 app.) filed on January 13, 2000, and the parent application (09/526,106) filed on March 15, 2000, of which the instant application is a continuation. Indeed, the Examiner has even acknowledged that support for the claims to the '106 and '968 applications is not in dispute. See, page 4, paragraph 4 of the Office Action mailed June 12, 2008. Applicants submit that the instant application is entitled to a priority date of at least March 15, 2000 (to the '106 application) in view of the Examiners acknowledgement that neither the '968 nor the '106 applications are in dispute.

In reply, please see the rejection above under paragraphs B and C which question the priority claim to the **'339** and ***'926*** applications and not the priority claim to the '968 and '106 applications.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 66, 71-77 and newly added 78-79 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claim 78 is confusing as to the when or where the first interactor domain begins and ends, especially in the absence of positive support in the specification and as applied to an oligopeptide of no less than 25 amino acids in length. [The claim is confusing absent any structures for the components of the fragment. The art has consistently identified (or characterized) compounds (peptides) by its structure and function. Thus the description of the oligopeptide fragment in words provide for confusion and ambiguity as to e.g., the kind of residues of oligopeptide from the N or C end, the beginning or terminating residues of a fragment absent formula of the parent protein. It is suggested that applicants incorporate the peptide structure of claim 66 to claim 78].

3. Claim 79 is unclear as to the C-terminal residues of the N-fragment being Glu 197 when the first and second fragments bind with one another and thus the termini of the fragments would be non-existent. Cf. with claim 66 structure.

Outstanding Objections and/or Rejections

Claims Rejections - 35 U.S.C. § 102

Claims 66, 71 and 72 are rejected under 35 U.S.C. 102(b) as being anticipated by Wehrman et al. (Wehrman et al. "Protein-protein interactions monitored in mammalian cells via complementation of β-lactamase enzyme fragments" *PNAS* **March 19, 2002**, *99(6)*, 3469-3474) (3/18/04 IDS, AB) for reasons of record as reiterated below.

> For ***claims 78 and 79***, Wehrman et al. disclose a fragment complementation system (e.g., see Wehrman et al., title wherein a β-lactamase complementation system is disclosed). In addition, Wehrman et al. disclose a first oligopeptide sequence and a second oligopeptide sequence wherein said first oligopeptide sequence is a fusion protein comprised of, in the direction of translation, an N-terminal fragment of a Class A β-lactamase protein no less than 25 amino acids in length fused through a first break point terminus to a first flexible polypeptide linker and a first interactor domain (e.g., see figure

1A; see also page 3470, column 2, second to last paragraph wherein the "197 β-lactamase fragment was fused to the amino terminus of the Fos helix [i.e., an interactor domain]"; see also figure 1 showing use of $(Gly_4Ser)_3$ linkers). Wehrman et al. also disclose a said second oligopeptide sequence that is a fusion protein comprised of, in the direction of translation, a second interactor domain and a second flexible polypeptide linker fused through a second break point terminus to a C terminal fragment of a class A β-lactamase protein not less than 25 amino acids in length (e.g., see figure 1A; see also page 3470, column 2, second to last paragraph wherein the "198 fragment fused to the carboxyl terminus of the Jun helix [i.e., an interactor domain]"; see also figure 1 showing use of $(Gly_4Ser)_3$ linkers). In addition, Wehrman et al. disclose wherein said first and second break-point termini are between 2 amino acids residues in a solvent exposed loop between amino acid residues Thr 195 and Ala 202 (e.g., see figure 1 wherein 197/198 junction is disclosed). Finally, Wehrman et al. disclose wherein upon binding of said first interactor domain with said second interactor domain said N-terminal fragment and said C-terminal fragment reconstitute to form a functional class A β-lactamase protein (e.g., see abstract; see also Results section; see also figures 2-4).

For ***claim 66***, Wehrman et al. disclose fragment complementation wherein said Class A β-lactamase protein comprises SEQ ID NO 2 with the E197/L198 junction (e.g., see figure 1).

For ***claim 71***, Wehrman et al. disclose the fragment complementation system of claim 63, wherein said first polypeptide linker is 3-30 amino acids in length; and wherein said second polypeptide linker is 3-30 amino acids in length (e.g., see figure 1; see also page 3470, column 2, second to last paragraph wherein the $(Gly_4Ser)_3$ linker is disclosed for each).

For ***claim 72***, Wehrman et al. disclose the fragment complementation system of 71 further comprising a first complementation enhancement peptide fused between the N-terminal fragment of the Class A β-lactamase protein and the first polypeptide linker and a second complementation enhancement peptide fused between the C-terminal fragment of the Class A β-lactamase protein and the second polypeptide linker (e.g., see page 3471, column 1, paragraph 1; see also page 3470, column 2, last two paragraphs wherein HSE, GRE, EKR, and NGR are disclosed).

Response to Arguments

Applicant's arguments directed to the above 35 U.S.C. § 102 rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the reasons set forth below.

Applicants argue, "The claims as presently amended are supported by at least the ('106 app.) as indicated above … [Therefore,] Wehrman et al. is not prior art … ."

In reply, Applicants have not been afforded priority as discussed above and, as a result, Applicants' arguments are moot.

Accordingly, the 35 U.S.C. § 102 rejection cited above is hereby maintained.

Claims Rejections - 35 U.S.C. § 102/103

Claims 78 and 79, 66, and 71 are rejected under 35 U.S.C. § 102(e) as anticipated by or, in the alternative, 35 U.S.C. § 103(a) as being unpatentable over Michnick et al. (U.S. Patent No. 6,828,099) (Filed May 31, 2001) alone or in view of Galarneau et al. (Galarneau et al., "β-Lactamase protein fragment complementation assays as *in vivo* and *in vitro* sensors of protein-protein interactions" *Nature Biotechnology* **2002**, *20*, 619-622) as further evidenced if necessary by Applicants' Exhibit 1 filed 10/25/06.

For ***claims 78 and 79***, Michnick et al. (see entire document) disclose a fragment complementation system (e.g., see Michnick et al., abstract), which anticipates the claimed invention. For example, Michnick et al. disclose a first oligopeptide sequence and a second oligopeptide sequence wherein said first oligopeptide sequence is a fusion protein comprised of, in the direction of translation, an N terminal fragment of a Class A β-lactamase protein no less than 25 amino acids in length fused through a first break point terminus to a first flexible polypeptide linker and a first interactor domain (e.g., see Example 2 wherein FRB-5a.a.-BLF[1] is disclosed, in this scenario FRB = interactor domain and BLF[1] = 23-197 of TEM-1 β-lactamase fragment and the 5 amino acids represents the linker). In addition, Michnick et al. disclose a second oligopeptide sequence that is a fusion protein comprised of, in the direction of translation, a second interactor domain and a second flexible polypeptide linker fused through a second break point terminus to a C-terminal fragment of a class A β-lactamase protein no less than 25 amino acids in length (e.g., see Example 2 wherein FKBP-5a.a.-BLF[2] is disclosed, in this scenario FKBP is the interactor domain and BLF[2] = 198-286 of TEM-1 β-lactamase fragment and the 5 a.a. represents the linker). Michnick et al. do not explicitly disclose the limitation "in the direction of translation" for either fragment, however, both the orientation disclosed in Michnick et al. and the opposite orientation as disclosed by Galarneau et al. (e.g., see figure 2 of Galarneau et al. wherein a 15 amino acid linker was used to connect to two fragments with the claimed orientation instead of two interactor domains) would be immediately envisioned because these are the "only two" orientations

that preserve protein folding as exemplified, for example, by Applicants' exhibit 1 (submitted 10/25/06). That is, protein folding is only preserved when a linker or pair of interactor domains bind to the same side of the protein (i.e. see exhibit 1, top figure), not to opposite ends (i.e., see exhibit 1, bottom figure). Therefore, a person of skill in the art would immediately envision both the "insert" and "circular permutation" orientations. *In re Petering* 133 USPQ 275 (CCPA 1962); see also *In re Schauman*, 572 F.2d 312, 197 USPQ 5 (CCPA 1978); see also MPEP § 2131. Alternatively, Michnick et al. inherently disclose this feature in accordance with *In re Graves*, 69 F.3d 1147, 36 USPQ2d 1697 (Fed. Cir. 1995) (prior art reference disclosing a system for testing the integrity of electrical interconnections that did not specifically disclose simultaneous monitoring of output points still anticipated claimed invention if simultaneous monitoring is within the knowledge of a skilled artisan). Here, fusions in the claimed orientation are shown to be within the knowledge of a skilled artisan by Galarneau et al. (e.g., see Galarneau et al., figure 2) showing the proper orientation in the QI construct using linker instead of a pair of interactor domains. In addition, Michnick et al. disclose wherein said first and second break-point are between 2 amino acid residues in a solvent exposed loop between amino acid residues Thr 195 and Ala 202 (e.g., see Example 2 wherein the break-point is at positions 197/198, see also column 2, lines 17-33 indicating that positions 196-200 form a solvent exposed loop; see also figure 1). Finally, Michnick et al. disclose binding of said first interactor domain with said second interactor domain said N terminal fragment and said C-terminal fragment reconstitute to form a functional class A β-lactamase protein (e.g., see figure 4; see also column 3, first full paragraph; see also column 5, lines 43-54).

For ***claim 66***, Michnick et al. also disclose a Class A β-lactamase protein comprises SEQ ID NO 2 (e.g., see Example 2; see also column 1, line 33 disclosing accession number AAB59737). Michnick et al. also disclose said first β-lactamase protein break-point and said second B-lactamase protein break-point are within 10 amino acids in either direction from a junction between 2 amino acid residues in SEQ ID NO 2 selected from the group consisting of P149 and N150 El72 and L173 K190 and V191 A202 and G203 and G228 and K229 (e.g., see Example 2 wherein the 197/198 break-point is disclosed that is within 10 amino acids of K190/V191 or A202/G203).

For ***claim 71***, Michnick et al. also disclose a fragment complementation wherein said first oligopeptide further comprises a first polypeptide linker that separates the N-terminal fragment of a β-lactamase protein from the first interactor domain wherein said first polypeptide linker is 3-30 amino acids in length and said second oligopeptide further comprises a second polypeptide linker that separates the C-terminal fragment of a Class A β-lactamase protein from the second interactor domain wherein said second polypeptide linker is 3-30 amino acids in length (e.g., see Example 2 disclosing the 5 amino acid linker Gly-Gly-Gly-Gly-Ser in each case).

In the alternative that the prior art teachings of Michnick et al. differ from the claimed invention, the difference is set forth as follows:

For ***claim 78,*** Michnick et al. fail to teach the a β-lactamase protein covalently bonded "through the C-terminus" of a β-lactamase protein break-point to a first interactor domain and a second oligopeptide comprising a C-terminal fragment of a Class A β-

lactamase protein covalently bonded "through the N-terminus" of a second class A β-lactamase protein break-point to a second interactor domain (i.e., this corresponds to the "insert" orientation disclosed in figure 2 of Galarneau et al. wherein a 15 amino acid linker was used to connect to two fragments with the claimed orientation instead of two interactor domains). To the contrary, Michnick et al. disclose just the opposite orientation (i.e., the "circular permutation" orientation, see Galarneau et al., figure 2) wherein a β-lactamase protein is covalently bonded "through the N-terminus" away from the first class A β-lactamase protein break-point to a first interactor domain and a second oligopeptide comprising a C-terminal fragment of a Class A β-lactamase protein is covalently bonded "through the C-terminus" of a second class A β-lactamase protein away from break-point to a second interactor domain.

However, Galarneau et al. teach the following limitations that are deficient in Michnick et al.:

For ***claim 78***, Galarneau et al. (see entire document) teach the use of rejoining the fragments (albeit with a linker instead of a pair of interactor domains) using the currently claimed orientation (e.g., see figure 2 wherein the QI construct possesses a linker that joins the BLF[1] fragment to he BLF[2] fragment at the 196/198 junction).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to join the interactor domains to the BLF[1] and BLF[2] fragments using their C- and N-termini, respectively (referred to as the "insert" orientation), because Galarneau et al. show that this orientation will not destroy the proper folding and hence activity of the enzyme (e.g., see figure 2, QI construct). Furthermore, a person of ordinary skill in the art would have been motivated to use this orientation instead of the reverse N- and C- termini for BLF[1] and BLF[2], respectively (referred to as the "circular permutation" orientation), because Galarneau et al. disclose that the "insert" orientation retains approximately 40% of the enzymes wild type activity whereas the "circular permutation" orientation retains only about 20% of the enzymes wild type activity (i.e., the "insert" activity is twice as good). Finally, a person of skill in the art would reasonably have expected to be successful because the "insert" orientation does not destroy the proper folding of the enzyme by "reversing" on of the subunits.

Response to Arguments

Applicants' arguments directed to the above 35 U.S.C. § 102/103 rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the reasons set forth below.

Applicants argue, "As indicated above, the claims as presently recited are supported by the priority documents … Therefore, the cited references are not prior art …."

The Examiner respectfully disagrees. As noted above, the priority documents do not provide the requisite support for the current claims, e.g., new claim 78, and, as a result, Applicants' arguments are moot.

Accordingly, the 35 U.S.C. § 102/103 rejection cited above is hereby maintained.

Claims Rejections - 35 U.S.C. § 112, first paragraph

Claims 78, 66, 71-77 and 79 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed had possession of the claimed invention for reasons of record and as applied to new claim 78..

New matter rejection

New claim 78, as added, is not supported in the as-filed specification Please see the rejection of claim 78 above, under the Priority Response paragraph A), which is a new matter rejection. In addition to the above, the claim to a "solvent" exposed loop between amino acid residues Thr 195 and Ala 202" that "reconstitute to form a functional β-lactamase protein" is not supported in the as-filed specification. The specification, as applicants stated above, reads "An exposed loop was identified by this method between two α-helixes of E. coli TEM-1 β-lactamase (approximately Thr195 to Ala 202, between helixes 7 and 8) within which the chain could be broken to produce fragments which could only complement for activity [i.e., reconstitute to form a functional lactamase] when fused to the fos and jun helixes." Thus, Applicants make clear in their specification that a functional enzyme for this loop will only result when fos/jun is used. Other

heterologous domains were disclosed in the following sentence including scfv, etc. but this applied only to the contiguous 197/198 junction, not the entire 195-202 loop. In addition, only TEM-1 β-lactamase of *E.coli* was used, not the currently claimed genus of β-lactamases from any source. For example, Wikipedia indicates that approximately 140 TEM-type enzymes are known including TEM-10, TEM-12, and TEM-26 (e.g., Wikipedia, the Free Encyclopedia. Beta-lactamase. Retrieved at http://en.wikipedia.org/wiki/Beta-lactamase on June 8, 2008, pages 1-11). In addition, as applicants state each of the lactamase can be broken down into numerous fragments. In addition, Applicants fail to describe any other. Further, Applicants admit that a thorough search of the fragment space is required to determine which fragments will reconstitute to form an active enzyme and cannot be determined by looking at the three dimensional structure of the molecule (e.g., see '926 priority document, page 4, last full paragraph, "However, the best fragments for such assisted complementation can not be found by examination of static 3-dimensional structures, but rather can only be found by conducting a thorough search of the 'fragment space' of the enzyme in question for fragments which perform in the desired manner under the desired conditions."). Further, Applicants' cited passages in the current application and priority documents (e.g., see 10/29/07 response, pages 9-11) fail to refute this position.

Response to Arguments

Applicants note that new independent claim 78 does not recite a first and second breakpoint, and thus the rejection does not apply. Likewise, claims 66 and 71-77 depend from 78 are likewise the rejection does not apply to the dependent claims.

In reply, new claim 78 does not obviate the rejection of claim 63 (note applicants' REMARKS (11/11/08) at page 7 that new claim 78 is similar to cancelled claim 63).

Please see the new matter rejection above under the priority claim paragraph A.

No claim is allowed.

Conclusion

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

/TERESA WESSENDORF/
Primary Examiner, Art Unit 1639